

In the claims:

Please amend the claims as follows:

1-15. (Cancelled)

16. (Currently amended) A method for identifying a member of a mass-coded combinatorial library which is a ligand for a first biomolecule, wherein the mass-coded combinatorial library is of the general formula  $XY_n$ ,  $n$  is an integer from 2 to about 6,  $X$  is a scaffold and each  $Y$  is, independently, a peripheral moiety, wherein each peripheral moiety is derived from a member of a peripheral moiety precursor subset, the method comprising the steps:

(a) choosing the peripheral moiety precursor subset comprising;

(i) choosing every set of two different peripheral moiety precursors from a peripheral moiety precursor set, said choosing performed in a manner such that for each set of two, if the two peripheral moiety precursors have equal molecular masses, then one of the two is removed, forming a remaining set;

(ii) from the remaining set, choosing every set of four peripheral moiety precursors, including for a given set of four, removing one of the four peripheral moiety precursors if a sum of the molecular masses of a first two precursors in the given set of four equals a sum of the molecular masses of a second two precursors in the given set of four peripheral moiety precursors, said choosing forming a remainder set;

(iii) from the remainder set, choosing every set of six different peripheral moiety precursors, including for a given set of six, removing one of the six peripheral moiety precursors if a sum of the molecular masses of a first three precursors in the given set of six equals a sum of the molecular masses of a second three precursors in the given set of six, said choosing forming a working selection set; and

(iv) from the working selection set of peripheral moiety precursors, choosing said peripheral moiety precursor subset such that said subset comprises a sufficient number of peripheral moiety precursors that there exist at least about 250 distinct combinations of  $n$  peripheral moieties derived from said subset, and wherein each of at least about 90% of the

combinations of n peripheral moieties has a molecular mass sum that is distinct from the molecular mass sum of all other combinations of n peripheral moieties derived from said subset;

(a~~b~~) contacting the first biomolecule with a~~the~~ mass-coded combinatorial library, said mass-coded combinatorial library comprising compounds of the general formula  $XY_n$ , wherein n is an integer from 2 to about 6, X is a scaffold and each Y is, independently, a peripheral moiety, wherein there exist at least about 250 distinct combinations of n peripheral moieties, and wherein each of at least about 90% of the combinations of n peripheral moieties has a molecular mass sum that is distinct from the molecular mass sum of all other combinations of n peripheral moieties, whereby members of the mass-coded combinatorial library which are ligands for the biomolecule bind to the first biomolecule to form first biomolecule-ligand complexes and members of the mass-coded library which are not ligands for the first biomolecule remain unbound;

(b~~c~~) separating the first biomolecule-ligand complexes from the unbound members of the mass-coded combinatorial library;

(e~~d~~) dissociating the first biomolecule-ligand complexes; and

(e~~e~~) determining the molecular mass of each ligand to identify the set of n peripheral moieties present in each ligand;  
wherein the molecular mass of each ligand corresponds to a set group of n peripheral moieties present in that ligand, thereby identifying a member of the mass-coded combinatorial library, which is a ligand for the first biomolecule.

17. (Original) The method of claim 16 wherein the biomolecule is immobilized on a solid support.

18. (Original) The method of claim 17 wherein the solid support is a water-insoluble matrix contained within a chromatographic column.

19. (Original) The method of claim 16 wherein a solution comprising the biomolecule is contacted with the mass-coded combinatorial library to form, if one or more

members of the combinatorial library are ligands for the biomolecule, a solution comprising biomolecule-ligand complexes and unbound members of the mass-coded combinatorial library.

20. (Original) The method of claim 19 wherein the unbound members of the mass-coded combinatorial library are separated from the biomolecule-ligand complexes by directing the solution comprising biomolecule-ligand complexes and the unbound members of the mass-coded combinatorial library through a size exclusion chromatography column, whereby the unbound members of the mass-coded combinatorial library elute from said column after the biomolecule-ligand complexes.

21. (Original) The method of claim 19 wherein the unbound members of the mass-coded combinatorial library are separated from the biomolecule-ligand complexes by contacting the solution comprising biomolecule-ligand complexes and the unbound members of the mass-coded combinatorial library with a size-exclusion membrane, whereby the unbound compounds pass through said membrane and the biomolecule-ligand complexes do not pass through said membrane.

22. (Original) The method of claim 16 wherein the biomolecule is a protein or a nucleic acid molecule.

23-53. (Cancelled)

54. (Withdrawn) The method of claim 16, further comprising the steps:

(e) contacting a second biomolecule with the mass-coded combinatorial library, whereby members of the mass-coded combinatorial library which are ligands for the second biomolecule bind to the second biomolecule to form second biomolecule-ligand complexes;

(f) separating the second biomolecule-ligand complexes from the unbound members of the mass-coded combinatorial library;

(g) dissociating the second biomolecule-ligand complexes;

(h) determining the molecular mass of each ligand for the second biomolecule; and

(i) determining which molecular mass or masses determined in step (d) are not determined in step (h), thereby providing the molecular masses of members of the mass coded combinatorial library which are ligands for the first biomolecule but are not ligands for the second biomolecule;

wherein each molecular mass determined in step (i) corresponds to a set of n peripheral moieties present in a ligand for the first biomolecule which is not a ligand for the second biomolecule, thereby identifying a member of the mass-coded combinatorial library which are ligands for the first biomolecule but are not ligands for the second biomolecule.

55. (Withdrawn) The method of claim 54 wherein the first biomolecule and the second biomolecule are each, independently, a protein or a nucleic acid molecule.

56. (Withdrawn) The method of claim 55 wherein the first biomolecule and the second biomolecule are each a protein, and the amino acid sequence of the second biomolecule are each a protein, and the amino acid sequence of the second biomolecule is derived from the amino acid sequence of the first biomolecule by insertion, deletion or substitution of one or more amino acid residues.

57. (Withdrawn) The method of claim 55 wherein the first biomolecule is a first protein and the second biomolecule is a second protein, said first and second proteins having the same amino acid sequence, wherein said first and second proteins have different posttranslational modifications.

58. (Withdrawn) The method of claim 57 wherein the first protein differs from the second protein in extent of phosphorylation, glycosylation or ubiquitination.

59. (Withdrawn) The method of claim 55 wherein the second biomolecule is a complex of the first biomolecule with a ligand.

60. (Withdrawn) The method of claim 55 wherein the first biomolecule and the second biomolecule are each immobilized on a solid support.

61. (Withdrawn) The method of claim 55 wherein the first biomolecule and the second biomolecule are each immobilized on a solid support.

62. (Withdrawn) The method of claim 55, wherein one or both of steps (b) and (f) is performed by contacting a solution comprising first biomolecule-ligand complexes or second biomolecule-ligand complexes and unbound members of the mass-coded combinatorial library with a size exclusion chromatography column, whereby the unbound members of the mass-coded combinatorial library elute from the column after the first biomolecule-ligand complexes or the second biomolecule-ligand complexes.

63. (Withdrawn) The method of claim 55, wherein one or both of steps (b) and (f) is performed by contacting a solution comprising first biomolecule-ligand complexes or second biomolecule-ligand complexes and unbound members of the mass-coded combinatorial library with a size exclusion membrane, whereby the members of the mass-coded combinatorial library pass through said membrane and the first biomolecule-ligand complexes or second biomolecule-ligand complexes do not pass through said membrane.

64-72. (Cancelled)

73. (New) A method for identifying a member of a mass-coded combinatorial library which is a ligand for a first biomolecule, wherein the mass-coded combinatorial library is of the general formula  $XY_n$ ,  $n$  is an integer from 2 to about 6,  $X$  is a scaffold and each  $Y$  is, independently, a peripheral moiety, the method comprising the steps:

- (a) producing the mass-coded combinatorial library, comprising
  - (i) choosing every set of two different peripheral moiety precursors from a peripheral moiety precursor set, said choosing performed in a manner such that for each

set of two, if the two peripheral moiety precursors have equal molecular masses, then one of the two is removed, forming a remaining set;

(ii) from the remaining set, choosing every set of four peripheral moiety precursors, including for a given set of four, removing one of the four peripheral moiety precursors if a sum of the molecular masses of a first two precursors in the given set of four equals a sum of the molecular masses of a second two precursors in the given set of four peripheral moiety precursors, said choosing forming a remainder set;

(iii) from the remainder set, choosing every set of six different peripheral moiety precursors, including for a given set of six, removing one of the six peripheral moiety precursors if a sum of the molecular masses of a first three precursors in the given set of six equals a sum of the molecular masses of a second three precursors in the given set of six, said choosing forming a working selection set; and

(iv) from the working selection set of peripheral moiety precursors, choosing said peripheral moiety precursor subset such that said subset comprises a sufficient number of peripheral moiety precursors that there exist at least about 250 distinct combinations of  $n$  peripheral moieties derived from said subset, wherein each of at least about 90% of the combinations of  $n$  peripheral moieties derived from said subset have molecular mass sums that are distinct from the molecular mass sum of all other combinations of  $n$  peripheral moieties derived from said subset; and

(v) contacting said peripheral moiety precursor subset with a scaffold precursor, said scaffold precursor having  $n$  reactive groups, wherein each reactive group is capable of reacting with at least one peripheral moiety precursor to form a covalent bond, under conditions sufficient for the reaction of each reactive group with a peripheral moiety precursor, thereby producing the mass-coded combinatorial library;

(b) contacting the first biomolecule with the mass-coded combinatorial library, whereby members of the mass-coded combinatorial library which are ligands for the biomolecule bind to the first biomolecule to form first biomolecule-ligand complexes and members of the mass-coded library which are not ligands for the first biomolecule remain unbound;

(c) separating the first biomolecule-ligand complexes from the unbound members of the mass-coded combinatorial library;

(d) dissociating the first biomolecule-ligand complexes; and

(e) determining the molecular mass of each ligand to identify the set of n peripheral moieties present in each ligand;

wherein the molecular mass of each ligand corresponds to a group of n peripheral moieties present in that ligand, thereby identifying a member of the mass-coded combinatorial library, which is a ligand for the first biomolecule.

74. (New) The method of claim 73, wherein the scaffold precursor is contacted with all members of the peripheral moiety precursor subset simultaneously.

75. (New) The method of claim 74, wherein the scaffold precursor is contacted with a solution comprising each member of the peripheral moiety precursor subset in approximately equal concentrations.

76. (New) The method of claim 73, wherein the scaffold precursor is contacted with the members of the peripheral moiety precursor subset sequentially.